

**AMENDMENTS TO THE CLAIMS**

**Claim 1 (withdrawn):** A method of reducing the systemic release of radioactive decay intermediates upon administration of a beta-emitting radionuclide to an individual, comprising the steps of:

incorporating said radionuclide into a large number of liposomes having a diameter sufficient to reduce the amount of radioactive decay intermediates; and

administering said large liposomes to said individual, wherein the presence of said radionuclide within said large liposomes reduces the systemic release of radioactive decay intermediates by said radionuclide.

**Claim 2 (withdrawn):** The method of claim 1, further comprising:

entrapping said radionuclide within smaller size liposomes prior to incorporating said radionuclide contained within said smaller size liposomes into said larger liposome.

**Claim 3 (withdrawn):** The method of claim 2, further comprising:

labeling said smaller liposomes.

**Claim 4 (withdrawn):** The method of claim 3, further comprising the step of:

coating outer membrane surfaces of said smaller size liposomes with molecules which preferentially associate with a specific target cell, thereby increasing specificity of said large liposomes to said target cell.

**Claim 5 (withdrawn):** The method of claim 4, wherein said target cell is a cancer cell, a virally infected cell, an autoimmune cell, or a cell expressing a receptor.

**Claim 6 (withdrawn):** The method of claim 4, wherein said molecules are antibodies, peptides, engineered molecules or fragments thereof.

**Claim 7 (withdrawn):** The method of claim 6, wherein said antibodies are Herceptin.

**Claim 8 (withdrawn):** The method of claim 1, further comprising the steps of:

preinjecting the individual with empty large liposomes; saturating the reticuloendothelial organs with said empty large liposomes; and injecting said radioactive tracer upon administration of said tracer.

**Claim 9 (withdrawn):** The method of claim 1, further comprising the steps of: said large liposomes have a diameter of about 900 nm to 1000 nm.

**Claim 10 (withdrawn):** The method of claim 1, further comprising the steps of: said large liposomes comprise molecules incorporated into or attached thereto which are capable of facilitating uptake by target cells.

**Claim 11 (withdrawn):** The method of claim 1, further comprising the steps of: said stabilizing molecules are polyethyleneglycol-linked lipids (PEG).

**Claim 12 (withdrawn):** The method of claim 1, further comprising the steps of: said stabilizing molecules further comprise an antibody, peptide, or antigenic fragment thereof attached thereto.

**Claim 13 (withdrawn):** The method of claim 1, further comprising the steps of: said large liposomes comprise a stabilizing agent incorporated into the aqueous phase with a high pH thereby further facilitating uptake by target cells of radioactive decay intermediates.

**Claim 14 (withdrawn):** The method of claim 1, further comprising the steps of: said stabilizing agent is a phosphate buffer, insoluble metal binding protein, chelating molecules or halogen binding molecules.

**Claim 15 (withdrawn):** The method of claim 1, further comprising the steps of: said large liposomes comprise additional molecules which facilitate interaction with target cells or facilitating endocytosis of the radioactive tracer.

**Claim 16 (withdrawn):** The method of claim 1, wherein said alpha particle-emitting radionuclide is incorporated into the aqueous phase of a liposomal compound.

**Claim 17 (withdrawn):** The method of claim 1, wherein said alpha particle-emitting radionuclide is 225Ac, 223Ra, 213Bi, or 213Po.

**Claim 18 (withdrawn):** The method of claim 1, wherein said alpha particle-emitting radionuclide is a daughter of a beta particle-emitting radionuclide; and wherein said beta particle-emitting radionuclide is incorporated into the aqueous phase of a liposomal compound.

**Claim 19 (withdrawn):** The method of claim 1, wherein said beta particle-emitting radionuclide is 212Pb.

**Claim 20 (currently amended):** A method for selectively targeting an individual for liposomal delivery of an alpha particle-emitting radionuclide, comprising:

entrapping passively said radionuclide in smaller liposomal vesicles; incorporating said entrapped radionuclide into larger liposomal vesicles, said liposomes having a diameter sufficient to reduce systemic release of radioactive decay intermediates of said radionuclide; polyethyleneglyco-linked liposomes; and

a targeting agent attached to the surface of said larger liposomal vesicles; and

delivering said radionuclide to the individual, such that said targeting agent targets said individual cells while retaining said larger liposomal vesicles, thereby target the cells while retention within said large liposomal vesicles of radioactive decay intermediates produced by said radionuclide minimizes damage to healthy tissue.

**Claim 21 (original):** The method of claim 20, further comprising labeling said smaller liposomal vesicles with a radioactive tracer.

**Claim 22 (original):** The method of claim 20, further comprising steps of:

preinjecting the individual with a monoclonal antibody specific for

saturating the non-endothelial organs to reduce non-tumor specific spleen and liver uptake of said radionuclides upon delivery.

**Claim 23 (original):** The method of claim 1, wherein said large liposomes have a diameter of about 0.5 μm to about 1.5 μm.

**Claim 24 (original):** The method of claim 1, wherein said targeting agents are antibodies, peptides, oligopeptides, or carbohydrates.

**Claim 25 (original):** The method of claim 1, wherein some of said antibodies are Herceptin.

**Claim 26 (original):** The method of claim 1, wherein said targeted cells are cancer cells, virally infected cells, or cells expressing a receptor.

**Claim 27 (original):** The method of claim 1, wherein said large liposomes further comprise a stabilizing agent, said agent being an aqueous phase with a high pH thereby further reducing the formation of radioactive decay intermediates.

**Claim 28 (original):** The method of claim 1, wherein said metal chelating agent is a phosphate buffer, insoluble metal complex, metal-binding molecules or halogen binding molecules.

**Claim 29 (original):** The method of claim 1, wherein said large liposomes further comprise additional molecules, said molecules facilitating fusion with target cells or facilitating endocytosis.

**Claim 30 (original):** The method of claim 1, wherein said alpha-particle emitting radionuclide is incorporated into the walls of said liposomal vesicles as a chelation compound.

**Claim 31 (original):** The method of claim 1, wherein said alpha-particle-emitting radionuclide is  $^{225}\text{Ac}$ ,  $^{223}\text{Ra}$ ,  $^{210}\text{Bi}$ , or  $^{211}\text{At}$ .

**Claim 32 (original):** The method of claim 1, wherein said alpha particle-emitting radionuclide is a member of a beta particle-emitting radionuclide, and wherein said beta particle-emitting radionuclide is entrapped within said liposomal vesicles.

**Claim 33 (original):** The method of claim 1, wherein said beta particle-emitting radionuclide is  $^{220}\text{Po}$ .

**Claim 34 (withdrawn):** A method of selectively targeting cells expressing HER-2/neu protein in an individual for localized treatment, comprising steps of:

entrapping said Ac-225 within said liposomes, said liposomes incorporating said entrapped Ac-225 and having reduced systemic release of radioactive decay intermediates of Ac-225; preparing polyethyleneglycol-linked Herceptin antibodies which bind to outer membranes thereof; and

Herceptin antibodies attached to the outer membranes of said liposomes, said Herceptin antibodies selectively targeting said cells expressing the HER-2/neu protein expressed on the cells, thereby selectively delivering said Ac-225 to the cancer cells, and reducing the systemic release of said radioactive decay intermediates produced by said radioactive decay of Ac-225, thereby reducing the systemic release thereof.

**Claim 35 (withdrawn):** The method of claim 1, further comprising labeling said smaller liposomes with a radioactive tracer.

**Claim 36 (withdrawn):** The method of claim 1, further comprising steps of:

preinjecting the individual with empty liposomes; saturating the reticuloendothelial organs with said empty liposomes; and measuring the spleen and liver uptake of said radionuclide upon administration of said radioactive tracer.

**Claim 37 (withdrawn):** The method of claim 1, wherein said large liposomes have a diameter of about 100 nm to about 1000 nm.

**Claim 38 (withdrawn):** The method of claim 1, wherein said target cells comprise an ovarian carcinoma.

**Claim 39 (withdrawn):** The method of claim 1, wherein said large liposomes further comprise a stabilizing agent in the aqueous phase with a high pH thereby further facilitating radioactive decay intermediates.

**Claim 40 (withdrawn):** The method of claim 1, wherein said stabilizing agent is a phosphate buffer, insoluble metal bonds, metal chelating molecules or halogen binding molecules.

**Claim 41 (withdrawn):** The method of claim 1, wherein said large liposomes further comprise additional molecules for enhancing membrane fusion with target cells or facilitating endocytosis.

**Claim 42 (withdrawn):** The method of claim 1, wherein Ac-225 is chelated.

**Claim 43 (withdrawn):** An alpha emitting radionuclide containing radionuclide, comprising:

    said alpha particle emitting radionuclide; and  
    small liposome vesicles entrapping said alpha emitting radionuclide; and

    a large liposome incorporating said alpha emitting radionuclide; wherein the large liposome having a diameter sufficient to retain at least some of the radioactive decay products of the alpha emitting radionuclide; and wherein the small liposomes are entrapped by the large liposome.

**Claim 44 (withdrawn):** The encapsulated radionuclide of claim 43, comprising:

    labeling said smaller liposomal vesicles;

Claim 45 (withdrawn): The encapsulated composition of claim 43, wherein said alpha particle emitting radionuclide is  $^{212}\text{Po}$ ,  $^{212}\text{Pb}$ , or  $^{211}\text{At}$ .

Claim 46 (withdrawn): The encapsulated composition of claim 39, wherein said alpha particle-emitting radionuclide associates with a beta particle-emitting radionuclide, wherein said beta particle-

Claim 47 (withdrawn): The encapsulated composition of claim 46, wherein said beta particle-emitting radionuclide-

Claim 48 (withdrawn): The encapsulated composition of claim 43, wherein said radionuclide associates with a molecule which is incorporated into the aqueous compartment of a liposome or is chelated by a chelating compound.

Claim 49 (withdrawn): The method of claim 43, wherein said large liposomes have a diameter of about 200 nm to 1000 nm.

Claim 50 (withdrawn): The encapsulated composition of claim 43, wherein said large liposomes further comprise molecules which associate with a target cell, said molecules coating outer surfaces of said liposomes.

Claim 51 (withdrawn): The method of claim 43, wherein said molecules are antibodies, polypeptides, or fragments thereof.

Claim 52 (withdrawn): The encapsulated composition of claim 43, wherein at least some of said antibodies are monoclonal antibodies.

**Claim 53 (withdrawn):** The encapsulated product of claim 50, wherein said target cell is a cancer cell, a normally infected cell, or an inflammatory cell.

**Claim 54 (withdrawn):** The encapsulated product of claim 43, wherein said large liposomes further comprise stabilizing molecules which bind to outer membranes to stabilize said large liposomes.

**Claim 55 (withdrawn):** The method of claim 43, wherein said stabilizing molecules further comprise an antibody, antigen, or fragment thereof attached thereto.

**Claim 56 (withdrawn):** The encapsulated product of claim 54, wherein said stabilizing molecules are polymethacrylates (polymers).

**Claim 57 (withdrawn):** The encapsulated product of claim 43, wherein said large liposomes comprise a stabilizing agent which bind to or have an aqueous phase with a high pH.

**Claim 58 (withdrawn):** The encapsulated product of claim 57, wherein said stabilizing agent is a phosphorus compound, a crosslinking polymer, resin beads, metal-binding molecules or thiol groups.

**Claim 59 (withdrawn):** The encapsulated product of claim 43, wherein said large liposomes comprise molecules which bind to or bind with a target cell or facilitating endocytosis by a target cell.